

1. A method for site-specific chemical modification of an HIV gp41-derived peptide during synthesis of the peptide, wherein the synthesized peptide has one or more amino acids having a side chain amine, the method comprising incorporating into the peptide, or a fragment thereof, during synthesis:

5           (a) at least one amino acid selected to have its side chain amine chemically reacted with a chemical protecting agent which protects the side chain amine from subsequent chemically reactivity with an amine-reactive functionality; and

10          (b) at least one amino acid having an amine unprotected and free for reacting with an amine-reactive functionality, wherein the free amine is selected from the group consisting of an N-terminal amine, a side chain amine, and a combination thereof.

2. The method according to claim 1, wherein the HIV gp41-derived peptide is synthesized by covalently coupling two or more fragments to produce the synthesized peptide; and wherein incorporated into at least one of the fragments is an amino acid having a side chain amine chemically reacted with a chemical protecting agent.

15          3. The method according to claim 1, wherein the HIV gp41-derived peptide is a peptide having an amino acid sequence of any one of SEQ ID NOs: 1-175, or an amino acid sequence having at least 95% identity with any one or more of SEQ ID NOs: 1-175.

20          4. The method according to claim 1, wherein the chemical protecting agent is selected from the group consisting of 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)ethyl, 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)-3-methylbutyl, allyloxycarbonyl, benzyloxycarbonyl, and 2-chlorobenzyloxycarbonyl.

25          5. The method according to any one of claims 1, 2, 3, or 4, wherein an amino acid having its side chain amine chemically reacted with a chemical protecting agent is lysine.

30          6. The method according to any one of claims 1, 2, 3, or 4, wherein a side chain amine that is chemically reacted with a chemical protecting agent is an epsilon amine.

35          7. An isolated HIV gp41-derived peptide having one or more amino acids containing a side chain amine, wherein at least one amino acid has its side chain amine chemically reacted with a chemical protecting agent which protects the side chain amine from subsequent chemically reactivity with an amine-reactive functionality; and at least one amino acid of the peptide has an amine unprotected and free for reacting with an amine-reactive functionality, wherein the free amine is selected from the group consisting of an

N-terminal amine, a side chain amine, and a combination thereof.

8. The HIV gp41-derived peptide according to claim 7, wherein the peptide is a peptide having an amino acid sequence of any one of SEQ ID NOs: 1-175, or an amino acid

5 sequence having at least 95% identity with any one or more of SEQ ID NOs: 1-175.

9. The HIV gp41-derived peptide according to claim 7, wherein the chemical protecting agent is selected from the group consisting of 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)ethyl, 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)-3-methylbutyl,

10 allyloxycarbonyl, benzyloxycarbonyl, and 2-chlorobenzylloxycarbonyl.

10. The HIV gp41-derived peptide according to any one of claims 7, 8, or 9, wherein the amino acid having its side chain amine chemically reacted with a chemical protecting agent is lysine.

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11. The HIV gp41-derived peptide according to any one of claims 7, 8, or 9, wherein the side chain amine that has been chemically reacted with a chemical protecting agent is an epsilon amine.

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12. A method for producing a substantially homogeneous conjugate comprised of HIV gp41-derived peptide and polymer, the method comprising:

(a) synthesizing an HIV gp41-derived peptide having one or more amino acids containing a side chain amine so that at least one amino acid is selected to have its side chain amine chemically reacted with a chemical protecting agent which protects the side chain amine from subsequent chemically reactivity with an amine-reactive functionality, and at least one amino acid of the peptide has an amine unprotected and free for reacting with an amine-reactive functionality, wherein the free amine is selected from the group consisting of an N-terminal amine, a side chain amine, and a combination thereof; and

(b) covalently coupling a polymer to the HIV gp41-derived peptide by chemically reacting an amine-reactive functionality of the polymer to a free amine group of the HIV gp41-derived peptide, wherein polymer is covalently coupled only to the one or more amino acids having a free amine, and not to the at least one amino acid protected by the chemical protecting agent, in producing the substantially homogeneous conjugate.

35 13. The method according to claim 12, wherein the conjugate comprises an HIV gp41 derived peptide covalently coupled to more than one molecule of polymer, wherein each molecule of polymer is coupled to an amino acid of the HIV gp41-derived peptide.

14. The method according to claim 12, wherein the method further comprises removing the chemical protecting agent from the substantially homogeneous conjugate.

15. The method according to claim 12, wherein the HIV gp41-derived peptide is synthesized by covalently coupling two or more fragments to produce the synthesized peptide; and wherein incorporated into at least one of the fragments is an amino acid having a side chain amine chemically reacted with a chemical protecting agent.

16. The method according to claim 12, wherein the HIV gp41-derived peptide is a peptide having an amino acid sequence of any one of SEQ ID NOs: 1-175, or an amino acid sequence having at least 95% identity with any one or more of SEQ ID NOs: 1-175.

17. The method according to claim 12, wherein the chemical protecting agent is selected from the group consisting of 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)ethyl, 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)-3-methylbutyl, allyloxycarbonyl, benzyloxycarbonyl, and 2-chlorobenzyloxycarbonyl.

18. The method according to claim 12, wherein the polymer comprises polyethylene glycol.

19. The method according to any one of claims 12, 13, 14, 15, 16, 17, or 18, wherein an amino acid having its side chain amine chemically reacted with a chemical protecting agent is lysine.

20. The method according to any one of claims 12, 13, 14, 15, 16, 17, or 18, wherein a side chain amine that has been chemically reacted with a chemical protecting agent is an epsilon amine.

21. A substantially homogeneous conjugate comprised of HIV gp41-derived peptide and polymer produced according to the method of any one of claims 12, 13, 14, 15, 16, 17, or 18.

22. The substantially homogeneous conjugate comprised of HIV gp41-derived peptide and polymer according to claim 21, further comprising a pharmaceutically acceptable carrier.

23. Use of a substantially homogeneous conjugate comprised of HIV gp41-derived

peptide and polymer according to claim 21 as an active therapeutic substance in therapy of HIV infection.

24. Use of a substantially homogeneous conjugate comprised of HIV gp41-derived

5 peptide and polymer according to claim 22 as an active therapeutic substance in therapy of HIV infection.

25. The use of a substantially homogeneous conjugate comprised of HIV gp41-derived peptide and polymer according to any one of claims 23 or 24, wherein the substantially

10 homogeneous conjugate is used as a part of a therapeutic regimen containing one or more additional antiviral agents for therapy of HIV infection.

26. Use of a substantially homogeneous conjugate comprised of HIV gp41-derived peptide and polymer according to claim 21 for the manufacture of a medicament for a

15 therapeutic application comprising treatment of HIV.

27. A pharmaceutical composition comprising a substantially homogeneous conjugate comprised of HIV gp41-derived peptide and polymer according to claim 21.

20 28. A pharmaceutical composition comprised of a substantially homogeneous conjugate comprised of HIV gp41-derived peptide and polymer according to claim 22.

29. A method for inhibition of transmission of HIV to a cell, comprising adding to the virus and the cell an amount of substantially homogeneous conjugate comprised of HIV gp41-derived peptide and polymer according to claim 21 effective to inhibit infection of the cell by HIV.

30 30. A method for inhibition of transmission of HIV to a cell, comprising adding to the virus and the cell an amount of a pharmaceutical composition according to claim 27 effective to inhibit infection of the cell by HIV.

31. The method according to claim 29, wherein the substantially homogeneous conjugate is added as a component of a therapeutic regimen.

35 32. The method according to claim 30, wherein the pharmaceutical composition is added as a component of a therapeutic regimen.

33. A method for inhibiting HIV fusion, comprising contacting the virus, in the presence of a cell, with an amount of substantially homogeneous conjugate comprised of HIV gp41-derived peptide and polymer according to claim 21 effective to inhibit HIV fusion.

5     34. A method for inhibiting HIV fusion, comprising contacting the virus, in the presence of a cell, with an amount of a pharmaceutical composition according to claim 27 effective to inhibit HIV fusion.

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